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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,066	10/18/2001	Frederick M. Ausubel	00786/387003	3890
21559	7590	06/17/2005	EXAMINER	
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			PRIEBE, SCOTT DAVID	
			ART UNIT	PAPER NUMBER

1632

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/042,066

Applicant(s)

AUSUBEL ET AL.

Examiner

Scott D. Priebe, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 12-16 and 18 is/are rejected.
- 7) ☒ Claim(s) 6, 8-11, 17 and 19-22 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>20050307</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Prosecution on the merits of this application is reopened on claims 1-5 and 6 considered unpatentable for the reasons indicated below in view of prior art provided in the Information Disclosure Statement filed 3/7/05.

Applicant is advised that the Notice of Allowance mailed 12/3/04 is vacated. If the issue fee has already been paid, applicant may request a refund or request that the fee be credited to a deposit account. However, applicant may wait until the application is either found allowable or held abandoned. If allowed, upon receipt of a new Notice of Allowance, applicant may request that the previously submitted issue fee be applied. If abandoned, applicant may request refund or credit to a specified Deposit Account.

Information Disclosure Statement

The EP – Communication/Supplementary Search Report listed on the PTO-1449 filed 3/7/05 has been considered. However, it is not a foreign patent, as indicated on the PTO-1449, and has been crossed off. It will not be printed on the face of the patent should one issue. Should Applicant wish this document listed on the face of the patent, it should be listed properly on a PTO-1449 as an “Other Document” and include all of the pertinent citation information. The Labrousse reference had already been made of record in the Information Disclosure Statement of 2/27/04.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5, 12, 13, 15, and 16 are rejected under 35 U.S.C. 102(a) as anticipated by over Kurz et al. (Trends Microbiol. 8 (3): 142-144, March 2000).

Kurz is a review of using *C. elegans* as a model system for studying host-pathogen interactions. It discloses that *Pseudomonas aeruginosa*, such as strains PA14 and PAO1, and *Serratia marcesans* are pathogenic in *C. elegans* as well as in mammals. It discloses that *P. aeruginosa* kills *C. elegans* in one of two-ways depending on growth conditions: “fast killing” when the nematode is infected with the bacteria on high-osmolality medium due to expression of a toxin by PA14; and “slow killing” when the nematode is infected with the bacteria on minimal medium (page 142, col. 2; and page 143). Kurz discloses that this assay system has been used to screen mutant *P. aeruginosa* for reduced virulence, and to screen mutant *C. elegans* for increased or decreased resistance to *P. aeruginosa* “fast killing” (para. bridging pages 142-143). Kurz discloses that *C. elegans* mutants can be screened for those conferring enhanced or reduced resistance to bacterial pathogens in order to shed light on host defense mechanisms and the interaction between pathogen and host (page 144).

Claims 1, 2, 4, 5, 12, 13, 15, and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Tan et al. (Curr. Opin. Microbiol. 3: 29-34, Feb. 2000). This prior art reference is authored by only two of the four instant inventors, and thus the “inventive entity” of the prior art reference constitutes “others” under 35 U.S.C. 102(a).

Tan is a review of using *C. elegans* and *Pseudomonas aeruginosa* as a model system for studying host-pathogen interactions. Tan discloses that the model system can be used to identify pathogen-encoded virulence factors and host-encoded defense-response pathways (page 29, col. 1). Tan discloses that *P. aeruginosa* strain PA14 kills *C. elegans* in one of two-ways depending on growth conditions: “fast killing” when the nematode is infected with the bacteria on high-salt, rich medium due to expression of a toxin by PA14; and “slow killing” when the nematode is infected with the bacteria on low-salt medium. *P. aeruginosa* strains PA01 and SE59 kill *C. elegans* by a third mechanism. (See para. bridging pages 29-30). Tan discloses carrying out genetic screens of mutant *C. elegans* that exhibit either enhanced resistance or enhanced susceptibility to *P. aeruginosa* strain PA14, and that enhanced susceptibility mutants are readily isolated because eggs can be recovered from the carcasses of dead mutant *C. elegans* (page 31, col. 2). Tan discloses that the availability of mutant *C. elegans* and *P. aeruginosa*, in conjunction with genetic analysis, can be used to uncover specific interactions between bacterial virulence determinants and host responses. Tan discloses that mutant *C. elegans* that are sensitive to oxidative stress, e.g. *mev-1* or *rad-8*, or that with lesions in P-glycoprotein genes *pgp-1* and *pgp-3* are more susceptible to *P. aeruginosa* “fast killing” (page 32).

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Claims 1, 2, 4, 5, 12, 13, 15, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Mahajan-Miklos et al. (Cell 96: 47-56, Jan 1999).

Mahajan-Miklos discloses screening adult mutant *C. elegans* having mutations in *age-1*, *mev-1*, *rad-8*, or both *pgp-1* and *pgp-3* for altered susceptibility to “fast killing” by growth on *P. aeruginosa* PA14. (See pages 50-52). While the *age-1* mutant was found to be more resistant to “fast killing” than wild type, the *mev-1*, *rad-8*, and (*pgp-1*, *pgp-3*) mutants were found to be more sensitive to fast killing than was wild type.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3, 7, 14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Kurz et al. (Trends Microbiol. 8 (3): 142-144, March 2000) or Tan et al. (Curr. Opin.

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Microbiol. 3: 29-34, Feb. 2000) as applied to claims 1, 2, 4, 5, 12, 13, 15, and 16 above, and further in view of Tan et al. (Proc. Natl. Acad. Sci. USA 96: 2408-2413, Mar. 1999).

Kurz and Tan (2000) have been described above. Neither Kurz nor Tan (2000) explicitly teach to screen *C. elegans* mutants for reduced sensitivity to “slow killing” by a pathogen. However, both suggest screening *C. elegans* mutants in general for reduced resistance to a bacterial pathogen in order to shed light on host defense mechanisms and the interaction between pathogen and host, and that mutants had been screened for altered susceptibility to “fast killing” by *P. aeruginosa* PA14. Also, neither suggests screening mutagenized *C. elegans* N2 worms in the L4 stage.

However, Tan (1999) describes assays for “slow killing” of *C. elegans* by *P. aeruginosa* PA14 that are carried out using strain N2 in L4 stage for the assay (page 2408, col. 2, to page 2409, col. 1, first full para.), because the larval stages are more resistant to slow killing, which allows more nematode progeny to be produced, which increases the sensitivity of the assay (page 2411, col. 2). Although Tan (1999) focuses on screening of mutagenized *P. aeruginosa*, it also teaches that the screening method can be used in high-throughput genetic assays to identify host genes, as well as pathogen genes, involved in the pathogenic interaction between pathogen and host (page 2413, para. bridging cols. 1-2).

Therefore, it would have been obvious to one of skill in the art at the time the invention was made to have used L4 stage *C. elegans* N2, as taught by Tan (1999) in a screen for mutant *C. elegans* with higher susceptibility to *P. aeruginosa* PA14 under “slow killing” conditions in the methods of either Kurz or Tan (2000), because the higher resistance of larval worms increases the sensitivity of the “slow killing” assay, Tan (1999) suggests that the “slow killing”

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assay could be used in high-throughput genetic screens to identify host genes, as well as pathogen genes, that are involved in the pathogen-host interaction, and both Kurz and Tan (2000) suggested identifying mutants with increased susceptibility to pathogenic infection in general.

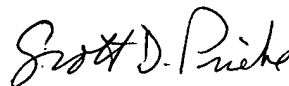
Allowable Subject Matter

Claims 6, 8-11, 17, and 19-22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Scott D. Priebe, Ph.D.
Primary Examiner
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